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Short Communications

Synthesis of 6-Deoxy-D-*galacto*-heptose

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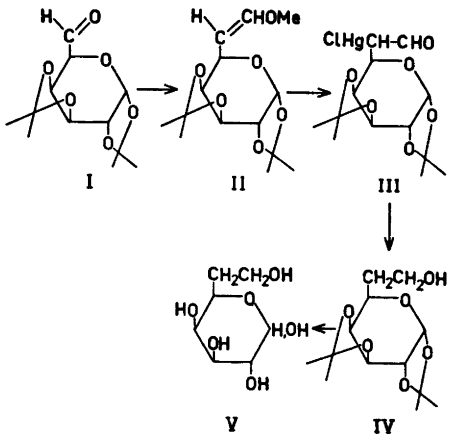
We recently established that 6-deoxy-D-*manno*-heptose is a component sugar of the *Yersinia (Pasteurella) pseudotuberculosis* group IIa lipopolysaccharide.[1] The identification of this sugar was confirmed by synthesis.[2] Several isomeric 6-deoxyhexoses have been found in Nature,[3] and are synthesized from nucleoside hexoses *via* the corresponding 6-deoxyhexos-4-ulose derivatives. It seems most probable that the 6-deoxy-D-*manno*-heptose is likewise synthesized from a nucleoside heptose. Other 6-deoxy-heptoses may also be found in Nature and the syntheses of these sugars is therefore a matter of some interest. 6-Deoxy-D-*gluco*-heptose, as the 1,2-*O*-isopropylidene derivative, was recently synthesized by Rosenthal and Kan [5] *via* the hydroformylation of 5,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose. We now report the synthesis of 6-deoxy-D-*galacto*-heptose.

The 6-deoxy-D-*galacto*-heptose was synthesized by a Wittig reaction, analogous to that used for the synthesis of the corresponding D-*manno* derivative.[2] The various synthetic transformations are outlined in Scheme 1. 1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose [6] was treated with methoxymethylenetriphenylphosphorane to afford the vinylic derivative II, which was transformed into the 7-aldehydo sugar III by treatment with mercuric chloride and mercuric oxide.[7] Reduction of III with sodium borohydride afforded the heptose derivative IV in an over-all yield of 10 % from I. Acid hydrolysis of IV produced 6-deoxy-D-*galacto*-heptose.



Scheme 1.

Experimental. General methods were the same as those described in a previous paper [2] NMR spectra, recorded for all compounds, except for III, were in accordance with the presumed structures.

*6-Deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galacto-heptopyranose (IV).* Methoxymethyltriphenylphosphonium chloride (6.7 g) in dry diethyl ether (44 ml) was enclosed in a serum bottle with a magnetic stirrer under nitrogen and cooled to −10°. Butyllithium (9.2 ml, 30 % in hexane) was added by syringe. The mixture was allowed to stand with stirring for 20 min. 1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (I) [6] (2.5 g) in dry diethyl ether (25 ml) at −10° was added by syringe and the mixture was allowed to stand with stirring under nitrogen for 1 h at −10° and then at room temperature for 18 h. Partitioning between diethyl ether and water, drying the diethyl ether solution over sodium sulphate, filtration and concentration afforded a crude syrup (II).

Crude, syrupy II was dissolved in acetone-water (10:1, 12 ml). Mercuric oxide (360 mg) was added with magnetic stirring and then, dropwise, with stirring, mercuric chloride (360 mg) in acetone-water (10:1, 4.0 ml).[7] The reaction was monitored by TLC and interrupted after about 5 min at room temperature. The mixture was filtered, concentrated to dryness to yield syrupy, crude III which immediately was dissolved in ethanol (15 ml); the ethanol solution was diluted with water to near turbidity. Exess sodium borohydride was added and the solution was allowed to stand at room temperature overnight. Sodium cations were removed with Dowex 50 (H^+ form). Filtration, concentration and repeated concentrations with methanol in order to remove boric acid as methyl borate afforded a syrup which after purification on silica gel [diethyl ether-light petroleum (40 – 60°)] gave chromatographically pure IV (260 mg), $[\alpha]_D$ −44° (*c* 0.6, $CHCl_3$). (Found: C 56.8; H 8.28, $C_{13}H_{22}O_6$ requires: C 56.9; H 8.08).

6-Deoxy-D-galacto-*heptose (V)*. The above di-*O*-isopropylidene derivative IV (39 mg) was treated with trifluoracetic acid-water [8] (9:1, 10 ml) at room temperature for 5 min. The solution was concentrated and the product dissolved in water, filtered and concentrated to a syrup (27 mg) $[\alpha]_D + 75°$ (*c* 0.9, H_2O). An aliquot of the material was transformed into 6-deoxy-D-*galacto*-heptitol hexaacetate by reduction with sodium borohydride followed by acetylation.[9] The GLC retention time relative to that of D-glucitol hexa-acetate (3 % ECNSS-M on Gas-Chrom Q at 180° and a flow rate of 30 ml/min) was 1.35. Another aliquot was reduced with sodium borodeuteride and then converted into the hexamethyl ether. The MS of the resulting 6-deoxy-1-deuterio-1,2,3,4,5,7-hexa-*O*-methyl-D *galacto*-heptitol showed the following (primary) fragments: *m/e* 235, 191, 178, 147, 134, 103, 90, 46, and 45. The remainder of the spectrum was in accordance with the presumed structure. The above 6-deoxy-D-*galacto*-heptitol hexaacetate crystallized, m.p. 123–125°, $[\alpha]_D$ −9° (*c* 0.4, $CHCl_3$). (Found: C 50.7; H 6.29. $C_{19}H_{28}O_{12}$ requires: C 50.9; H 6.29).

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The Structure of Methyl β-D-Ribopyranoside

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X-Ray crystallographic studies on the pyranose form of aldopentoses [1–6] have shown that the structures agree with those predicted by Reeves.[7] Thus, β-arabinose,[1–3] β-lyxose,[4] and α-xylose,[5,6] are found to have the conversion forms 1*a*2*e*3*e*4*a*, 1*e*2*a*3*e*4*e*, and 1*a*2*e*3*e*4*e*, respectively.

As regards the fourth aldopentose, ribose, preliminary crystallographic data only have been reported.[8] However, a structure study of 2-deoxy-β-ribose has been carried out.[9]

The conversion form 1*a*3*e*4*a* which 2-deoxy-β-ribose has in the crystalline state, does not agree with Reeves' predictions, and it has been proposed in this connection that an axial substituent on C(1) should be regarded as an element of stability rather than an element of instability.[9] An X-ray structure study of methyl β-ribopyranoside which may occur as 1*a*2*a*3*e*4*a* or 1*e*2*e*3*a*4*e*, was therefore thought of interest.

The results from this study show, *cf.* Fig. 1, that methyl β-D-ribopyranoside in the crystalline state has the conversion form 1*a*2*a*3*e*4*a*, which from Reeves' stability scheme [7] is supposed to be the least stable one.

One may query, however, whether the assumed stabilizing effect of the 1*a* substituent has been decisive for the structure in this case. There is namely an intramolecular hydrogen bond between O(2) and O(4) which at least to some degree stabilizes the molecule. Similar intramolecular hydrogen bonds occur in methyl 1-thio-β-D-ribopyranoside and methyl 1,5-dithio-β-D-ribopyranoside,[10] and the possibility for such bonding should therefore be taken into account when judging about the stability of the conversion forms of pyranoses. It should be mentioned in this connection that methyl 5-thio-β-D-ribopyranoside occurs as 1*e*2*e*3*a*4*e* in the crystalline state.[11]

The C–O and C–C bond lengths in methyl β-D-ribopyranoside, as derived from the coordinates in Table 1, are shown in Fig. 1. The values agree with those reported by James and Stevens from an independent X-ray study of the compound,[12] and also with those previously reported for glycoside structures.[13,14]

The three hydroxyl hydrogens participate in hydrogen bonds. They are, O(2)···O(4) = 2.77 Å with H(O2)···O(4) = 2.09 Å, O(3)···O(2)′ = 2.85 Å with H(O3)···O(2)′ = 2.03 Å, and O(4)···O(3)′ = 2.87 Å with H(O4)···O(3)′ = 2.22 Å. Thus each of the hydroxyl oxygens donates as well as accepts a hydrogen bond.

Methyl β-D-ribopyranoside crystallizes from ethyl acetate,[15] as orthorhombic prisms elon-